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Benign childhood epilepsy with Centro-Temporal spikes (BCECTSs), electrical status epilepticus in sleep (ESES), and academic decline — How aggressive should we be?

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ABSTRACT

Since many of the children with BCECTSs display electrical status epilepticus during sleep and many present with different comorbidities, mainly ADHD and behavioral disturbances, clinicians are often confronted with the dilemma of how aggressive they should be with their efforts of normalizing the EEG. We conducted a retrospective study by screening medical records of all consecutive patients with BCECTSs, spike–wave index (SWI) >30%, and ADHD/ADD that were evaluated in our pediatric epilepsy service and were followed up for at least two years. Patients with neurocognitive deterioration detected by formal testing were excluded. A total of 17 patients with mean age of 6.9 years at BCECTS diagnosis were identified. The patients' mean SWI was 60% and that dense electrical activity lasted 1.5 years on average (range: 1–4.5 years). Six children were formally diagnosed with learning disabilities in addition to ADD/ADHD. All of them were treated with an average of three antiepileptic medications, mainly for the purpose of normalizing the EEG, but none of them was treated with steroids or high-dose diazepam. The mean duration of follow-up was 5.5 years. A cognitive or behavioral deterioration was not detected in any of them. Our data suggest that when treating a child with BCECTSs, high SWI, and school difficulties, the most critical parameter that determines the necessity of using second-line antiepileptic agents such as steroids or high-dose diazepam is a formal psychological evaluation that proves cognitive (I.Q.) decline. Otherwise, these agents may be avoided.

1. Introduction

Benign childhood epilepsy with centrotemporal spikes (BCECTSs) is a frequent partial idiopathic syndrome of early school years. The syndrome is also called rolandic epilepsy because of the characteristic features of partial seizures involving the region around the lower portion of the rolandic fissure. Benign childhood epilepsy with centrotemporal spikes is the most frequent of the benign focal epilepsies of childhood and represents 15% to 25% of epilepsy syndromes in children under 15 years of age [1]. The age at onset ranges from 3 to 13 years, with the peak incidence occurring between ages 7 and 8 years [2]. The seizures are characterized by hemifacial motor seizures and may be preceded by somatosensory symptoms involving the inner cheek, tongue, and lips [3,4]. They frequently involve the hand or both the hand and the leg on the ipsilateral side to the facial involvement [4,5]. The seizures usually occur during sleep but may also occur during the daytime.

Most patients run a benign course, while few present with atypical evolution including Landau–Kleffner syndrome, electrical status epilepticus in sleep (ESES), classic atypical BCECTSs, and other forms [6,7]. In addition, many patients present with comorbidities such as attention deficit hyperactivity disorder (ADHD), learning disabilities, and behavioral disorder [8–13].

The evolution of BCECTSs to ESES had been previously described in detail [14–16], with a frequency range of 1.3–4.6% in large cohorts of consecutive patients [7,17].

Epileptic encephalopathy with status epilepticus in sleep (ESES) was first described in 1971 and was further classified several years later by Tassinari et al. [18–20]. According to the last International League Against Epilepsy proposal [21], the syndrome is defined as an age-related self-limited disorder characterized as epilepsy with different seizure types, neuropsychological impairment in the form of global or selective regression of cognitive functions, motor impairment, and typical EEG findings of continuous epileptic activity occupying ≥85% of non-REM sleep. The minimal spike–wave index (SWI) required for

Abbreviations: BCECTSs, benign childhood epilepsy with centrotemporal spikes; ESES, electrical status epilepticus in sleep; SWI, spike–wave index; EEG, electroencephalogram; ADD, attention deficit disorder; ADHD, attention deficit hyperactivity disorder; AED, antiepileptic drug; REM, rapid eye movement; I.Q., intelligence quotient.

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the definition of ESES in recent studies is 30% [22]. The term "continuous spikes and waves during slow sleep" is synonymous for ESES. Three studies reported the incidence of ESES as being 0.2–0.6% of all childhood epilepsies [23,24].

While the long-term outcome of epilepsy in ESES has been shown to be favorable, with seizures disappearing in almost all cases [25], the prognosis is, nevertheless, guarded because of the persistence of severe neuropsychological and/or motor deficits in approximately half of the patients [23,26,27].

Resolution of ESES had been achieved with conventional antiepileptic drugs (AEDs) including ethosuximide [28,29], valproic acid [25,30], benzodiazepines [22,30–32], levetiracetam [17,33,34], and sulthiame [17,22]. When these agents fail to normalize the EEG, a trial with second-line agents such as steroids [17,25–27] or high-dose diazepam [35,36] is attempted.

Since many of the children with BCECTSs display electrical ESES during sleep and many present with different comorbidities, mainly ADHD and behavioral disturbances, clinicians are often confronted with the question of how aggressive they should be in their efforts of normalizing the EEG.

The purpose of this study were to present a consecutive cohort of patients with BECTSs, ESES, and academic difficulties without I.Q. deterioration and to reassure clinicians that aggressive second-line therapies can be avoided.

2. Material and methods

A retrospective database was screened for consecutive patients with BCECTSs between the years 2000 and 2011 from a single epilepsy clinic in a tertiary hospital. In this clinic, most patients with BCECTSs underwent sleep EEG. In cases where the awake EEG showed characteristic rolandic discharges and where there was no history of functional deterioration, sleep EEG was not considered mandatory. In most cases, daytime nap sleep EEG was considered sufficient unless the child could not sleep during the day due to hyperactivity. In these cases, a single night video-EEG was performed. The SWI was routinely documented in all sleep records by the two authors.

Sixteen-channel EEG recordings were performed in all children. The EEG technicians were requested to perform a prolonged daytime nap EEG. The author first looked at the full sleep recording and visually picked the epoch with the highest spike density. The counting began starting with a page (10 s) of a high spike density and continued for ten consecutive minutes. Each page was scored separately. Each second which contained spikes, either focal or generalized, was considered positive, and the total number of positive seconds per page was calculated as percents of the whole page. At the end of the counting, an average of 60 pages (10 min) was performed and then displayed in terms of the nearest ten percentile number (for example, 63.7% was changed to 60%) [37].

Attention deficit hyperactivity disorder symptomatology was either evaluated by pediatric neurologists according to DSM-IV criteria or diagnosed with formal psychological evaluations. The neuropsychological tests included the Wechsler Intelligence Scale for Children — Revised and the Kaufman Assessment Battery for Children [38].

Patients with characteristics similar to ESES and ADHD caused by an etiology other than BCECTSs, such as perinatal insult, were excluded from the analysis to enhance the homogeneity of the group. Patients who were diagnosed with ESES or had been treated with steroids prior to follow-up were excluded from the study.

All patients' files were reviewed by the authors, and data were retrospectively reviewed and analyzed: age of patient at the onset of epilepsy; length of follow-up; seizure history; SWI; age at which attention deficit was suspected; results of formal psychological/didactic evaluations; and utilization of methylphenidate: intended, refused, or utilized. The study was approved by the institutional review board.

3. Results

Sixty-eight patients with the diagnosis of BCECTSs were ascertained; twenty-one patients had awake EEG only. Twelve patients had sleep EEG with SWI of less than 30%, and 35 patients had SWI $\geq$ 30%. Twelve children were diagnosed with ESES (i.e., neuropsychological decline in the presence of ESES), leaving 23 patients with BCECTSs and high SWI but without ESES syndrome. Of those, an additional 6 patients were excluded: 4 patients were excluded because they did not manifest ADD/ADHD symptomatology, and 2 patients were excluded because of a short follow-up (1 year). The rest of the patients, 17 children in total, were analyzed further.

There were nine girls and eight boys with an average age of 6.9 $\pm$ 2 years at diagnosis of BCECTSs (range: 3.5–10 years). Two of them never experienced seizures (patient nos. 12 and 15), and one patient was diagnosed before the first seizures occurred (patient no. 5). The patients were diagnosed with high SWI (>30%) during non-REM sleep at an average age of 8 $\pm$ 2.2 years and that electrical activity lasted 1.5 $\pm$ 0.5 years on average (range: 1–4.5 years). The average density of epileptic activity during non-REM sleep was 60% $\pm$ 19.4% (range: 30–100%). All the children had ADHD/ADD at the time of diagnosis; six children were also diagnosed with learning disabilities. One patient had aggression, and other patients had behavioral problems, which required psychiatric medications. One boy had only ADHD and behavioral difficulties. Six patients were diagnosed with ADD/ADHD or speech difficulty during preschool years, long before the diagnosis of BCECTSs had been established. All patients were treated with an average of three antiepileptic medications that are accepted as a treatment for BCECTSs (Range: 1 to 6). Changes of AEDs were performed mainly for the purpose of normalizing the sleep EEG, but none of them was treated with steroids or high-dose diazepam.

The children were followed up for an average of 5.5 $\pm$ 2.8 years (range: 1–10.5 years). During the follow-up time, none of them showed any formal cognitive deterioration, although academic difficulties were apparent. Three children actually demonstrated improvement as was reflected in their school achievements and formal neurocognitive evaluations. Four patients still had the same dense electrical activity in the EEG (patient nos. 3, 6, 7, and 16).

4. Discussion

Benign childhood epilepsy with centrotemporal spikes is a benign disease. One of the known characteristics is the aggravation of interictal discharges reaching a significant density with SWI of more than 30% in a considerable number of patients. Another known characteristic of the disease is the high frequency of attention deficit disorder and learning disabilities among the patients [8,11–13,15,20]. This combination is a source for clinical debate in many of the patients regarding the correct treatment, the necessity to normalize the sleep interictal epileptic activity, and the effect of EEG normalization on the behavioral difficulties [39]. This debate is brought into focus mainly when the child displays academic decline, behavioral difficulties and even aggression. The clinician may wonder if the child is manifesting initial symptomatology of ESES and consider possible treatment with either steroids or high-dose diazepam. Since these agents are involved with partial success, on the one hand, and significant adverse reactions, on the other hand [36,40], the debate becomes complex. Attention deficit disorder/attention deficit hyperactivity disorder was depicted as an inclusion symptom for this specific cohort since this is a common symptom in this disease, which can usually be defined without formal didactic evaluation and, in most cases, leads to academic decline that prompts further investigation such as sleep EEG. In the absence of this symptom, the patients are not routinely evaluated for learning difficulties or undergo sleep EEG.

The children in the cohort represent a subgroup that neither follow the definitions for any of the atypical types of benign rolandic epilepsy

[4] nor display an early age at onset of seizures, which may be associated with a less favorable course [41,42]. No formal cognitive deterioration (i.e., I.Q. decline) was documented throughout the entire follow-up period among the patient population. To emphasize, the children in the cohort represent a subgroup of children with BCECTSs who present with the common combination of dense epileptic activity (≥30%) during non-REM sleep, ADHD, learning disabilities, and mild behavioral difficulties but without cognitive or severe behavioral deterioration that is required for the diagnosis of ESES. In this group of children, the ADHD/ADD and learning disabilities are a comorbidity of the BCECTSs with atypical features [43], and, despite the impressive epileptic activity, no significant regression occurred. The results support the data in previous studies that these children have a favorable outcome, which is not different from that of a child with classic BCECTSs [11]. Therefore, in this specific subgroup, an aggressive antiepileptic treatment should be withheld as long as the patients are closely monitored for signs of cognitive/behavioral deterioration. When there is a clinical suspicion for deterioration, a formal psychological evaluation should be performed (sometimes repeatedly) in order to reassure the physician that the patient does not progress towards the ESES syndrome.

The patients from the current cohort do not represent the typical distribution of severity of BCECTSs since the cohort is derived from an outpatient epilepsy clinic in a tertiary center. This fact does not, however, prevent us from discussing the specific, not rare group which is the target of the current debate: patients with BCECTSs with relatively high SWI and ADHD with or without behavioral difficulties but without I.Q. decline.

5. Conclusions

Our data suggest that when treating a child with BCECTSs, high SWI, and school difficulties, the most critical parameter that determines the necessity of using more aggressive antiepileptic agents such as steroids or high-dose diazepam is a formal psychological evaluation that proves cognitive decline.

Conflict of interest

I declare no conflict of interest.

References

[1] Fejerman N, Caraballo RH, Dalla Bernardina B. Atypical evolutions of benign childhood epilepsy with centrotemporal spikes. In: Fejerman N, Caraballo RH, editors. Benign focal epilepsies in infancy, childhood and adolescents. London, England: John Libbey, Eurotext Ltd.; 2007. p. 179.

[2] Kriz M, Grazdik M. Epilepsy with centrotemporal (rolandic) spikes: a peculiar seizure disorder of childhood. Neurol Neurochir Pol 1978;12:413–9.

[3] Lombroso CT. Sylvian seizures and mid-temporal spike foci in children. Arch Neurol 1967;17:52–9.

[4] Aicardi J. Benign rolandic epilepsy. Int Pediatr 1987;2:176–81.

[5] Loiseau P, Beaussart M. The seizures of benign childhood epilepsy with rolandic paroxysmal discharges. Epilepsia 1973;14:381–9.

[6] Panayiotopoulos CP. Benign childhood partial seizures and related epileptic syndromes. London: John Libbey; 1999 312–6.

[7] Fejerman N, Caraballo R, Tenenbaum SN. Atypical evolutions of benign localization-related epilepsies in children: are they predictable? Epilepsia 2000;41:380–90.

[8] Deonna T, Zesiger P, Davidoff V, Maeder M, Mayor C, Roulet E. Benign partial epilepsy of childhood: a longitudinal neuropsychological and EEG study of cognitive function. Dev Med Child Neurol 2000;42(9):595–603.

[9] Massa R, de Saint Martin A, Hirsch E, Marescaux C, Motte J, Seegmuller C, et al. Landau–Kleffner syndrome: sleep EEG characteristics at onset. Clin Neuropysiol 2000; 111(Suppl. 2):S87–93.

[10] Holtmann M, Matei A, Hellmann U, Becker K, Poustka F, Schmidt MH. Rolandic spikes increase impulsivity in ADHD — a neuropsychological pilot study. Brain Dev 2006;28(10):633–40.

[11] Datta A, Sinclair DB. Benign epilepsy of childhood with rolandic spikes: typical and atypical variants. Pediatr Neurol 2007;36(3):141–5.

[12] Goldberg-Stern H, Gonen OM, Sadeh M, Kivity S, Shuper A, Inbar D. Neuropsychological aspects of benign childhood epilepsy with centrotemporal spikes. Seizure 2010;19: 12–6.

[13] Tovia E, Goldberg-Stern H, Ben Zeev B, Heyman E, Watemberg N, Fattal Valevski A, et al. The prevalence of atypical presentations of benign childhood epilepsy with centrotemporal spikes. Epilepsia 2011:521483–8.

[14] Dalla Bernardina B. Partial epilepsies of childhood, bilateral synchronization continuous spike-wave during slow sleep. In: Manelis J, Bental E, Loeber JN, Dreifuss FE, editors. Advances in epileptology, XVII. New York: Raven Press; 1989. p. 295–302.

[15] Massa R, de Saint-Martin A, Carcangiu R, Rudolf G, Kleitz C, Metz-Lutz MN, et al. EEG criteria predictive of complicated evolution in idiopathic rolandic epilepsy. Neurology 2001;25(57(6)):1071–9.

[16] Tassinari CA, Rubboli G, Volpi L, Billard C, Bureau M. Electrical status epilepticus during slow sleep (ESES or CSWS) including acquire epileptic aphasia (Landau-Kleffner syndrome). In: Roger J, Bureau M, Dravet CH, editors. Epileptic syndromes in infancy, childhood and adolescence. John Libbey Eurotext; 2005. p. 295–314.

[17] Kramer U, Sagi L, Goldberg-Stern H, Zelnik N, Nissenkorn A, Ben-Zeev B. Clinical spectrum and medical treatment of patients with electrical status epilepticus in sleep (ESES). Epilepsia 2009;50:1517–24.

[18] Patry G, Laygoubi S, Tassinari CA. Subclinical "electrical status epilepticus" induced by sleep in children. Arch Neurol 1971;24:242–52.

[19] Tassinari CA, Dravet C, Roger J. Encephalopathy related to electrical status epilepticus during slow sleep. Electroeceph Clin Neurophysiol 1977;43:529–30.

[20] Tassinari CA, Rubboli G, Volpi L, Meletti S, d'Orsi G, Franca M, et al. Encephalopathy with electrical status epilepticus during slow sleep or ESES syndrome including acquired aphasia. Clin Neurophysiol 2000;111(Suppl. 2):S94–S102.

[21] Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. Epilepsia 2001;42:796–803.

[22] Liukkonen E, Kantola-Sorsa E, Paetau R, Gaily E, Peltola M, Granström ML. Long-term outcome of 32 children with encephalopathy with status epilepticus during sleep, or ESES syndrome. Epilepsia 2010;51(10):2023–32.

[23] Morikawa T, Seino M, Watanabe M, Yagi K. Clinical relevance of continuous spike-wave during slow sleep. In: Manelis S, Bental E, Loeber JN, Dreifus FE, editors. Advances in epileptology. New York: Raven Press; 1989. p. 359–63.

[24] Kramer U, Nevo Y, Neufeld MY, Fattal A, Leitner Y, Harel S. Epidemiology of epilepsy in childhood — a cohort of 440 consecutive patients. Ped Neurol 1998;18: 46–50.

[25] Guerrini R, Genton P, Bureau M, Parmeggiani A, Slas-Puig X, Santucci M. Multilobar polymicrogyria, intractable drop attack seizures and sleep related electrical status epilepticus. Neurology 1998;51:504–12.

[26] Billard C, Autret A, Laffont F, Lucas B, Degiovanni E. Electrical status epilepticus during sleep in children: a reappraisal from eight new cases. In: Sterman MB, Shouse MN, Passouant P, editors. Sleep and epilepsy. London & New-York: Academic Press; 1982. p. 481–91.

[27] Tassinari CA, Bureau M, Dravet C, Dalla Bernardina B, Roger J. Epilepsy with continuous spike and wave during slow sleep — otherwise described as ESES (epilepsy with electrical status epilepticus during slow sleep). In: Roger J, Bureau M, Dravet C, Genton P, Tassinari CA, Wolf P, editors. Epileptic syndromes in infancy, childhood and adolescence. London: John Libbey; 1992. p. 188–94.

[28] Roulet-Perez E, Davidoff V, Despland PA, Deonna T. Mental and behavioral deterioration of children with epilepsy and CSWS; acquired epileptic frontal syndrome. Dev Med Child Neurol 1993;35:661–74.

[29] Ming L, Xiao-Yu H, Jiong Q, Xi-Ru W. Correlation between SWS and aphasia in Landau–Kleffner syndrome: a study of three cases. Brain Dev 1996;18: 197–200.

[30] Inutsuka M, Kobayashi K, Oka M, Hattori J, Ohtsuka Y. Treatment of epilepsy with electrical status epilepticus during slow sleep and its related disorders. Brain Dev 2006;28:281–6.

[31] Boel M, Casaer P. Continuous spikes and waves during slow sleep: a 30 months follow-up study on neuropsychological recovery and EEG findings. Neuropediatrics 1989;20:176–80.

[32] Yasuhara A, Yoshida H, Hatanaka T, Sugimoto T, Kobashi Y, Dyken E. Epilepsy with continuous spike–wave during slow sleep and its treatment. Epilepsia 1991;32: 59–62.

[33] Capovilla G, Beccaria F, Cagdas S, Montagnini A, Segala R, Paganelli D. Efficacy of levetiracetam in pharmacoresistant continuous spikes and waves during slow sleep. Acta Neurol Scand 2004;110:144–7.

[34] Aeby A, Poznanski N, Verheulpen D, Wetzburger C, Van Bogaert P. Levetiracetam efficacy in epileptic syndromes with continuous spikes and waves during slow sleep: experience in 12 cases. Epilepsia 2005;46(12):1937–42.

[35] De Negri M, Baglietto MG, Battaglia FM, Gagerro R, Pessagno A, Recanati L. Treatment of electrical status epilepticus by short diazepam cycles after diazepam rectal bolus test. Brain Dev 1995;17:330–3.

[36] Sánchez Fernández I, Chapman K, Peters JM, Klehm J, Jackson MC, Berg AT, et al. Guidelines for EEG in encephalopathy related to ESES/CSWS in children. Epilepsia 2009;50(Suppl. 7):13–7.

[37] Scheltens-de Boer M. Guidelines for EEG in encephalopathy related to ESES/CSWS in children. Epilepsia 2009;50(Suppl. 7):13–7.

[38] Wechsler D. Wechsler Memory Scale — Revised. San Antonio, TX: Harcourt Brace Jovanovich; 1987.

[39] Schneebaum N, Goldberg-Stern H, Fattal-Valevski A, Kramer U. Does a normalizing the EEG in patients with BCECTS abort attention deficit hyperactivity disorder? Pediatr Neurol 2012;47:279–83.

[40] Kramer U, Watemberg N, Zelnik N, Shahar E, Lerman-Sagie T, Goldberg- Stern H, et al. Efficacy of steroid therapy in the treatment of epileptic encephalopathies and refractory epilepsies. J Ped Neurology 2006;4:147–53.
[41] Kramer U, Shahar E, Zelnik N, Lerman-Sagie T, Watemberg N, Nevo Y, et al. Carbamazepine versus sulthiame in treating benign childhood epilepsy with centrotemporal spikes. J Child Neurol 2002;17(12):914–6.
[42] Saltik S, Uluduz D, Cokar O, Demirbilek V, Dervent A. A clinical and EEG study on idiopathic partial epilepsies with evolution into ESES spectrum disorders. Epilepsia 2005;46(4):524–33.
[43] Verrotti A, Latini G, Trotta D, Giannuzzi R, Cutarella R, Morgese G, et al. Typical and atypical rolandic epilepsy in childhood: a follow-up study. Pediatr Neurol 2002; 26(1):26–9.